REMARKS

Claims 1-77 are pending. Claims 1, 5, 7, 12, 19, 32, and 76 are amended. Claims 42-72 are withdrawn. No new matter is added.

Formal Matters

The Office Action states that the specification is objected to because it contains nucleic acid sequences that are not properly identified by a sequence identifier number. A preliminary amendment was filed on May 5, 2004 to add sequence identifier numbers to the specific sequences referenced in the Office Action. Accordingly, as of May 5, 2004 the application was in full compliance with 37 C.F.R. §1.821-1.825. Applicants, therefore, request that the objection be reconsidered and withdrawn.

Rejection of Claims 5, 7, 12-20, 32, 38, 39 and 76 Under 35 U.S.C. §112, Second Paragraph

The Office Action states that claim 5 is rejected for reciting the phrase "wherein said tumor is derived" with insufficient antecedent basis. For the sake of clarity, the cited language is herewith amended to "wherein said tumor cell is derived".

The Office Action states that claim 7 is rejected for reciting the phrase "...wherein said fusion polypeptide is endogenous to said cell" The Office Action states that something which is endogenous to a cell must be naturally present in it, and that, since the recited fusion polypeptide is genetically engineered, it cannot be naturally present in a cell and therefore cannot be endogenous. Applicants respectfully submit that, on the contrary, "endogenous" denotes being expressed from within a cell OR being naturally present in it, the key feature being that it is not produced outside the cell (compare with the definition of "exogenous" in the specification). Nevertheless, solely for the sake of expediting prosecution, claim 7 is herewith amended to replace "endogenous to" with "expressed by".

The Office Action states that claim 12 and its dependent claims 13-20 are rejected on the grounds that the recitation "at least about 10", renders the claim

indefinite. Applicants respectfully disagree. Nevertheless, in order to expedite prosecution, Applicants are herewith amending claims 12 and 13-20 to remove the word "about".

The Office Action rejects claim 19 for illogically depending on claim 18. Applicants had intended claim 19 to depend on claim 15, and claim 19 is herewith amended to correct this typographical error.

The Office Action states that claims 32, 38, and dependent claim 39 are rejected on the grounds that the recitation "at least about five", renders the claim indefinite. Applicants respectfully disagree. Nevertheless, in order to expedite prosecution, Applicants are herewith amending claims 32, 38, and 39 to remove the word "about".

The Office Action states that claim 76 is rejected for the recitation of the term "some." Applicants traverse the rejection, since they submit that the claims clearly read on compositions in which any amount of the recited fusion polypeptide is not bound to the recited cell or virus. In the interest of expediting prosecution, though, Applicants are herewith amending claim 76 to read, "The composition of claim 1 which comprises said fusion polypeptide unbound to said antigen-bearing target."

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejections under §112, second paragraph.

Rejection of Claims 1-41, and 73-77 Under 35 U.S.C. §112, First Paragraph

Claims 1-41 and 73-77 have been rejected for allegedly failing to comply with the written description requirement of 35 U.S.C. 112, first paragraph. The Office Action states, "The state of the prior art is such that one of skill in the art would not know from the recitation of the claims in view of the specification, what would encompass the claimed genus...." Applicants respectfully disagree and, accordingly, traverse the rejection.

The compositions of the claimed invention comprise an antigen-bearing target and further comprise a fusion polypeptide with well-defined characteristics. With respect to the antigenic component, the specification clearly defines "antigen bearing target" (see specification paragraph 0005). Furthermore, the specification discloses a large, representative number of antigens (see paragraphs 0439-0452), as well as various types of antigen bearing targets (see, for example, paragraphs 0005, 0049, 0482-0484) that can be incorporated into the claimed compositions.

As defined in the specification, an "antigen" is "a molecule against which a subject can initiate a humoral and/or cellular immune response" (paragraph 0006). The immune response arises from similar processes, e.g. processing by antigen presenting cells and activation of lymphocytes, for a broad range of antigens. Accordingly, textbooks and manuals are filled with principles, observations, and methods that relate to "antigens", without regard to their origin or particular identity, so reference to a generalized antigen is conventional and of great utility in the art. This also explains at least in part why it is not necessary to limit the types of antigen bearing targets or antigens that may be incorporated into the instant invention, provided that all the recited elements are present. Furthermore, Applicants have filed, in connection with a co-pending application (Serial No. 10/666,886) a declaration by Andrew Segal under 37 C.F.R. §132, that shows three additional antigen-bearing cell types that can be used.

In the claimed invention, the recited fusion polypeptide comprises first and second portions with defined, limiting functions. With respect to the first amino acid sequence, the specification discloses a large, representative number of the recited moieties (e.g. paragraphs 0101-0143). Similarly, with respect to the second amino acid sequence, the specification teaches a representative number of examples (e.g. paragraphs 151-436). The specification also teaches assays that determine whether one molecule is a ligand for another (e.g. paragraphs 454-463), and similar assays, e.g. competitive binding assays, are routine and well-known to those skilled in the art.

Thus, each of the recited elements of the claimed invention is illustrated by a representative number of examples. Furthermore, each element is defined by a functional characteristic which is easily discernible to one skilled in the art.

Applicants note that the Office Action states that the recited ligands could encompass small molecules. Applicants respectfully submit that this is not the case, since polypeptides, which are recited, are distinct from small molecules.

The Office Action further states that "the recitation that an amino acid sequence "can" do something...is not a limitation to said amino acid sequence". The Office Action goes on to state, e.g., that any amino acid sequence imaginable can bind to the recited carbohydrates. It is unclear to Applicants why Examiner believes this. It is well known that some molecules (such as lectins and their respective carbohydrate targets) will associate and bind to each other on contact, while other molecules will not bind to each other. Accordingly, Applicants submit that the functional characteristics embodied in the recitation of claim elements are fully delimiting.

Applicants therefore respectfully request that Examiner withdraw all rejections that allege a failure to comply with the written description requirement of 35 U.S.C. 112, first paragraph.

Rejections Under 35 U.S.C. §102

Ali et al.

The Office Action states that claims 1-8, 10, 22, 24-30, 32, and 76 are rejected under §102(b) for lack of novelty over Ali et al as evidenced by Cantrell et al. The Office Action states that Ali et al teaches a fusion polypeptide of the instant invention admixed with M3 melanoma cells. Applicants believe that this statement misapprehends Ali et al and therefore respectfully traverse the rejection.

In fact, the Ali reference teaches a replication-defective HSV-2 virus that harbors in its genome a nucleic acid encoding GM-CSF. Upon infection, the nucleic acid is delivered to a target cell and GM-CSF is expressed in the cell. The reference does not teach a fusion polypeptide, i.e. a single, continuous polypeptide molecule comprising two or more heterologous amino acid sequences, at all.

The Office Action also states that HSV-2 constitutes an N-terminal amino acid sequence that can bind sialic acid. However, HSV-2 is a complex, multi-protein virus, rather than a single amino acid sequence that can be incorporated into a fusion polypeptide. Furthermore, the Office Action provides no basis for asserting that HSV-2 can bind to sialic acid.

Thus, Ali et al does not teach the requisite elements of the claimed invention. Cantrell et al teaches the amino acid sequence of GM-CSF, and does not correct the deficiencies of Ali et al. Therefore, even if combined, the references fail to anticipate the instant invention.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

Faulkner et al.

The Office Action rejects claims 1, 2, 6-8, 10-18, 20-22, 24-27, 34, 35, 37-41, and 75-77 under 35 U.S.C. §102 as being anticipated by Faulkner et al, as evidenced by the specification and Raymond et al. The Office Action states that Faulkner et al teaches fusion polypeptides of portions of influenza HA linked to IL-2 or GM-CSF. The Office Action further asserts that the HA peptides taught by Faulkner et al fall under the limitations of the carbohydrate binding domain recited in the claims. Applicants disagree and traverse the rejection.

The recited first amino acid sequence must by definition be able to bind carbohydrate as delimited by the claims. It is readily evident that the HA peptides taught by Faulkner et al cannot do so. Aytay and Schulze (1991, J. Virology 65: 3022) teach that the carbohydrate binding domain of HA consists of a shallow pocket present on the distal end of the HA1 subunit. The specific sialic acid binding region has also been identified. Weis et al. (1988, Nature 333: 426) teach that the binding site is a depression, the bottom of which is formed by the phenolic hydroxyl of Tyr 98 and the aromatic ring of Trp 153, that Glu 190 and Leu 194 project down to form a short alpha-helix to define the rear of the site with His 183 and Thr 155, and that residues 134 to 138 form the 'right' side of the site and residues 224 to 228 form the 'left' side. Moreover, various mutagenesis studies have been carried out to determine residues in

the binding pocket which are critical for SA binding (see, e.g., Nobusawa et al., 2000, Virology, 278:587; Martin et al., 1998, Virology 241:101; Nobusawa and Nakajima, 1988, Virology 167: 8; and Rogers et al., 1983, Nature 304: 76). It is thus known in the art that amino acids 98, 134-138, 153, 155, 183, 190, 194, and 224-228 of HA are critical for sialic acid binding.

The short HA peptide taught by Faulkner et al. has the sequence SFERFEIFPK and spans amino acid positions 110-119. Faulkner et al. also teaches a second HA peptide spanning positions 94-131. The peptides disclosed by Faulkner thus omit residues involved in and critical for carbohydrate binding. Thus, these peptides could not bind carbohydrate, and neither Faulkner nor the Office Action provides any evidence that they can do so. Raymond simply reports sequences of H1N1 influenza A HA1 domains, and therefore does not remedy the deficiencies of Faulkner et al

Therefore, the cited references do not teach all of the elements of the claimed invention. Accordingly, Faulkner et al. does not anticipate the instant claims and Applicants request that the rejection be reconsidered and withdrawn.

Hayashi et al.

The Office Action rejects claims 1, 2, 6, 7, 9, 10, 21, 23-27, 34, 36, 37, 38-41, and 76 as being anticipated by Hayashi et al under 35 U.S.C. §102(a). Specifically, the Office Action relies on the alleged fact that Hayashi et al teaches a fusion polypeptide comprising an amino acid sequence which can bind to sialic acid. Applicants disagree and traverse the rejection.

The Office Action states that human type III collagen is a first amino acid sequence that is incorporated into a fusion polypeptide taught by Hayashi et al, and that this amino acid sequence can bind to sialic acid. However, there is no support for the allegation that type III collagen can bind to sialic acid. In fact, type III collagen is not known to bind to sialic acid, nor does it otherwise fall under the limitations of the claims at issue.

Therefore, Hayashi et al fails to teach the essential claim elements and cannot be used as prior art against the instant invention under 35 U.S.C. §102(a). Applicants accordingly request that the rejection be withdrawn.

Ramshaw et al.

Claims 1, 2, 6-8, 10, 11-13, 20-22, 24-27, 34, 35, 37-41, and 76 are rejected under 35 U.S.C. §102(b) as being anticipated by Ramshaw et al. The Office Action states that Ramshaw et al teaches a fusion polypeptide of the instant invention, in which influenza hemagglutinin allegedly provides the first amino acid sequence and mouse IL-2 allegedly provides the second amino acid sequence. Applicants respectfully disagree, and therefore traverse the rejection.

Ramshaw et al., in fact, does not teach a fusion polypeptide at all. Although this reference teaches nucleic acid constructs that encode multiple amino acid sequences, they are expressed as separate molecules, rather than as a fusion polypeptide. This is expressly evident from the drawings of Ramshaw et al, especially Figure 6a. Moreover, Ramshaw et al. clearly states at column 7, lines 6-8, that the hemagglutinin and cytokine were coexpressed from the viral constructs, "but from separate sites in the viral genome." Thus, they are not combined in a fusion polypeptide.

In order to support a rejection under 35 U.S.C. §102, a reference must teach all elements of the claimed invention. Since a fusion polypeptide is an essential element of the claimed invention, and since Ramshaw et al fails to teach a fusion polypeptide, the '131 patent does not anticipate the instant claims.

Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claims 1, 2, 6-8, 10-22, 24-27, 34, 35, 37-41, and 75-77 Under 35 U.S.C. §103(a)

The Office Action has rejected claims 1, 2, 6-8, 10-22, 24-27, 34, 35, 37-41, and 75-77 under 35 U.S.C. §103(a) as being obvious over Faulkner et al. in view of Air, Raymond et al, and the specification. The Office Action applies Faulkner et al. as described above, and asserts that it would be obvious to combine Faulkner et al. with the teachings of Air relating to hemagglutinin influenza A to arrive at the claimed invention. Applicants traverse the rejection.

Applicants submit that the Office Action does not establish that the claimed invention is obvious over Faulkner et al in view of Raymond et al. In order to establish a *prima facie* case of obviousness, among other things, the prior art reference (or references when combined) must teach or suggest *all the claim limitations*. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). As explained in response to the 102(b) rejections hereinabove, Faulkner et al. fails to teach a fusion polypeptide which comprises a first amino acid sequence that falls within the carbohydrate-binding limitations of the claims. Such a fusion polypeptide is also not taught by Raymond et al or by any prior art referred to by the specification. Thus, even if combined, the cited references fail to teach all the elements of the claimed invention, and therefore do not obviate the instant claims.

Applicants further note that, prior to the instant invention, there would have been no motivation to substitute a sialic-acid binding sequence of HA for the short, non-binding sequences taught by Faulkner et al. First, Faulkner's intention was to use well-defined T cell epitopes. T cell epitopes are known in the art to be short peptides. Second, and moreover, Faulkner's hypothesis is that the cytokine moiety operates by targeting the chimeric protein to the specific, complementary cytokine receptor. Fusion to a sialic-acid binding sequence would be expected to interfere with this mechanism, since sialic acid is virtually ubiquitous on mammalian cell surfaces and the fusion polypeptide would thus bind non-specifically to cells.

In order to allege the obviousness of claim 19 , the Office Action relies on the combination of Faulkner et al with Air. However, Air does not teach the fusion polypeptide in which Faulkner at al is deficient. Thus, again, even if combined, the teachings of Faulkner et al. and Air to not teach each limitation of the instant claims, and do not render the claims obvious.

Based on the above considerations, Applicants respectfully request that the rejections be withdrawn.

Rejection of Claims 1-8, 10, 22, 24-33, and 76 Under 35 U.S.C. §103(a)

Claims 1-8, 10, 22, 24-30, 32, and 76 are rejected under 35 U.S.C. §103(a) as being obvious over Ali et al in view of Cantrell et al. Applicants traverse the rejection.

The Office Action advances the same arguments with respect to the alleged obviousness of claims 1-8, 10, 22, 24-30, 32, and 76 as it does with respect to their alleged lack of novelty. As set forth hereinabove in response to the corresponding 102(b) rejections, neither of the cited references teaches a fusion polypeptide. Therefore, even if combined the references do not teach or suggest all the limitations of the claimed invention and do not support a finding of obviousness. The same references are relied on to allege the obviousness of claims 31 and 33, both of which depend on claim 1, and again fail to teach the indispensible claim element of a fusion polypeptide.

Therefore, Applicants respectfully request that the rejections be withdrawn.

Rejection of Claims 1, 2, 6-8, 10-18, 20-22, 24-34, 35, 37-41, and 75-77 Under 35 U.S.C. §103(a)

Claims 1, 2, 6-8, 10-18, 20-22, 24-34, 35, 37-41, and 75-77 are rejected under 35 U.S.C. §103(a) for alleged obviousness over Faulkner et al in view of Cantrell et al, as evidenced by the specification and by Raymond et al. Applicants traverse the rejection.

As set forth hereinabove, none of the cited prior art references teach a fusion polypeptide which falls within the recited claim limitations. Therefore, they cannot properly be combined to establish the obviousness of the claimed invention.

Applicants accordingly request that the rejections be withdrawn.

Rejection of Claims 1-8, 10, 22, 24-30, 32, 73, 74 and 76 Under 35 U.S.C. §103(a)

Claims 1-8, 10, 22, 24-30, 32, 73, 74 and 76 are rejected under 35 U.S.C. §103(a) as being obvious over Ali et al in view of Natesan, as evidenced by Cantrell et al. Applicants traverse the rejection.

The arguments advanced for obviousness with respect to claims 1-8, 10, 22, 24-30, 32, 73, and 76 are apparently the same as those advanced for the lack of novelty of those claims, and depend solely on the Ali and Cantrell references. As discussed hereinabove, these references, even if combined, do not provide the essential claim elements, and so do not suffice to establish obviousness of the claimed invention.

The Office Action further cites Natesan for the purpose of alleging obviousness of claim 74. Natesan teaches chimeric constructs comprising transcriptional activators, which may further comprise linker sequences. However, Natesan does not teach fusion polypeptides with first and second amino acid sequences falling within the functional limitations imposed by the instant claims. Hence, even if Natesan is combined with Ali et al. and Cantrell et al., the references collectively fail to provide all of the requisite claim elements and do not support a *prima facie* finding of obviousness.

Applicants accordingly request that the rejections be withdrawn.

Rejection of Claims 1, 2, 6-8, 10-18, 20-22, 24-27, 34, 35, 37-41, and 73-77 Under 35 U.S.C. §103(a)

Claims 1, 2, 6-8, 10-18, 20-22, 24-27, 34, 35, 37-41, and 73-77 are rejected under 35 U.S.C. §103(a) for obviousness over Faulkner et al in view of Natesan et al, as evidenced by the specification and Raymond et al. Applicants traverse the rejection.

As set forth hereinabove, none of the cited references teaches a fusion polypeptide that falls within the instant claims. Accordingly, even if combined, the references do not teach or suggest each element of the claimed invention and, thus, do not support a finding of obviousness.

Therefore, Applicants request that the rejections be withdrawn.

Rejection of Claims 1, 2, 6-8, 10, 11-13, 20-22, 24-27, 34, 35, 37-41, and 76 Under 35 U.S.C. §103(a)

Claims 1, 2, 6-8, 10, 11-13, 20-22, 24-27, 34, 35, 37-41, and 76 are rejected under 35 U.S.C. §103(a) as being obvious over Ramshaw et al in view of Natesan et al. Applicants traverse the rejection.

As discussed hereinabove, neither of the cited references teaches a fusion polypeptide that falls within the claims' recited limitations. Indeed, Ramshaw et al does not teach a fusion polypeptide at all. Thus, even if combined, the cited references fail to provide the requisite claim elements and, thus, do not support a finding of obviousness.

Therefore, Applicants request that the rejections be withdrawn.

Double Patenting

The Office Action states that the instant claims are provisionally unpatentable under the judicially-created doctrine of obviousness-type double patenting in view of several copending patent applications. Applicants will consider filing a terminal disclaimer to obviate this rejection upon notification of otherwise allowable subject matter in the instant claims.

In view of the above amendments and remarks, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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